1. B.K., a 65-year-old, 75 kg male, was admitted to the coronary care unit with a diagnosis of acute myocardial infarction. He has a history of mild chronic renal failure, but he does not have CHF. His serum creatinine of 1.5mg/dL. He has developed premature ventricular contractions (PVCs) which were unresponsive to lidocaine. Calculate a parenteral loading dose of procainamide designed to achieve a plasma concentration of around 8 mg/L and an i.v. maintenance infusion rate that will maintain an average plasma concentration of 6mg/L. (10 points)

A.) Loading Dose = 1200 mg; Maintenance infusion rate = 184 mg/min
B.) Loading Dose = 1200 mg; Maintenance infusion rate = 3.1 mg/min
C.) Loading Dose = 1400 mg; Maintenance infusion rate = 184 mg/min
D.) Loading Dose = 1400 mg; Maintenance infusion rate = 3.1 mg/min
E.) Loading Dose = 1200 mg; Maintenance infusion rate = 21.4 mg/hr

\[ V_d = 2 \cdot 75 = 150L \]
\[ LD = \frac{C_p \cdot V_d}{F \cdot S} = \frac{8 \cdot 150}{1 \cdot 0.87} = 1379mg \approx 1400mg \]

\[ CL_{Cr} = \frac{(140 - 65) \cdot 75}{72 \cdot 1.5} = 52.1mL/\text{min} \approx 3.1L/h \]

\[ CL_{renal} = 3 \cdot 3.1 = 9.4L/h \]
\[ CL_{acet} = 0.13 \cdot 75 = 9.75L/h \]
\[ Cl_{other} = 0.1 \cdot 75 = 7.5L/\text{hr} \]
\[ CL_{total} = 9.4 + 9.75 + 7.5 = 26.65L/h \]

\[ MD = \frac{C_{ss,ave} \cdot CL \cdot \tau}{F \cdot S} = \frac{6 \cdot 26.65 \cdot 1}{1 \cdot 0.87} = 183.8mg \approx 184mg/\text{hr} = 3.1mg/\text{min} \]
2. G.A. is a 20 year old 55.25kg female receiving an aminophylline drip which is started at a rate of 35mg aminophylline/h. An i.v. loading bolus of 750mg aminophylline was administered at the beginning of the therapy. Drug levels obtained at the end of 1st and 7th hours produce results of 19 mg/L and 15 mg/L, respectively. Calculate a dose of aminophylline to maintain a theophylline level of 15 mg/L for constant IV infusion.

(10 points)

a. 42.5mg/h  

b. 50mg/h  

c. 56mg/h  

d. 65mg/h  

e. 70mg/h

\[
\text{Cl} = \frac{2R_0}{(C_1 + C_2)} + \frac{2V_d(C_1 - C_2)}{(C_1 + C_2)(t_2 - t_1)} \\
= \frac{2 \times 0.85 \times 35}{(19 + 15)} + \frac{2 \times 0.5 \times 55.25(19 - 15)}{(19 + 15)(7 - 1)} \\
= 2.83 \text{L/h}
\]

\[
R_0 = \frac{C_{pss} \times \text{Cl}}{F} = \frac{15 \times 2.83}{0.85} = 50 \text{mg/h}
\]

Another accepted answer would be:

\[
V_d = S \times F \times \text{Loading Dose}/C_1 = (0.8 \times 1 \times 750 \text{ mg})/19 \text{ mg/L} = 31.6 \text{ L}
\]

\[
\text{Cl} = \frac{2R_0}{(C_1 + C_2)} + \frac{2V_d(C_1 - C_2)}{(C_1 + C_2)(t_2 - t_1)} \\
= \frac{2 \times 0.8 \times 35}{(19 + 15)} + \frac{2 \times 31.6 \text{ L} \times (19 - 15)}{(19 + 15)(7 - 1)} = 2.88 \text{ L/hr}
\]

\[
R_0 = \frac{C_{pss} \times \text{Cl}}{S} = \frac{15 \times 2.8}{0.8} = 54 \text{ mg/h} \approx 56 \text{ mg/hr}
\]
3. H.K., 55 year old, 5’2”, 70 kg woman with a serum creatinine of 1.6 mg/dL, has been empirically started on 500 mg of vancomycin every 12 hours for treatment of a staphylococcal infection. What are the expected peak and trough vancomycin concentrations for H.K? (10 points)

Key:

First, the Vd, Cl and ke must be calculated:

For the Vd,

\[ Vd = 0.17(55 \text{ years}) + 0.22(70 \text{ kg}) + 15 = 39.75 \text{ L} \]

Creatinine clearance can be used to estimate her clearance, but we must first check if the patient is obese:

IBW = 45.5 + 2.3*2 = 50.1

IBW*1.2 = 45.5 + 2.3*2 = 50.1*1.2 = 60.12

Since the patient is obese, we use the ABW for the CL calculation:

\[ ABW = IBW + 0.4(TBW-IBW) = 50.1 + 0.4(19.9) = 58.06 \]

\[ Clcr = \frac{(140-55)*58.06}{85*1.6} = 36.29 \text{ mL/min} = 2.18 \text{ L/h} \]

Now ke can be determined:

\[ Ke = 2.18/39.75 = 0.055 \text{ h}^{-1} \]

Now you can determine peak and trough concentrations

\[ Css_{\text{max}} = \frac{500/39.75}{(1 - e^{-0.055*12})} = 26.03 \text{ mg/L} \]

\[ Css_{\text{min}} = 26.03e^{-0.055*12} = 13.45 \text{ mg/L} \]

***DUE TO A TYPO IN THE ORIGINAL ANSWER KEY ALL ANSWERS WILL BE MARKED CORRECT***
4. L.E., an 80 kg male patient (6'2", 52 y.o., SeCr 1.0 mg/dl), received a 30 mg methotrexate loading dose iv followed by a 25 mg/h infusion over 36 hours. At 36 h, leucovorin rescue (10 mg/m² q6h ) was started. The following levels were monitored:

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Methotrexate Level (μM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 h</td>
<td>14</td>
</tr>
<tr>
<td>48 h</td>
<td>0.8</td>
</tr>
<tr>
<td>60 h</td>
<td>0.3</td>
</tr>
</tbody>
</table>

When do you expect the methotrexate level to fall below 0.1 μM? (10 points)

A. 57 hr  
B. 81.5 hr  
C. 64.5 hr  
D. 71.5 hr  
E. 87 hr

Solution:

\[ k_\alpha = \frac{\ln(14)}{0.8} = 0.239 \]

\[ t_{1/2} = 2.9 \text{ h} \]

For 0.5 μM:

\[ t = \frac{\ln(0.5)}{0.237} = 13.9 \text{ h} \rightarrow 49.9 \text{ hr} \]

\[ k_\beta = \frac{\ln(0.5/0.3)}{10.1} = 0.051 \text{ h}^{-1} \rightarrow t_{1/2\beta} = 13.6 \text{ h} \]

\[ t_{0.1\mu M} = \frac{\ln(0.3/0.1)}{0.051 \text{ h}^{-1}} = 21.5 \text{ h} + 60 \text{ hr} = 81.5 \text{ hr} \]
5. DB is a 56 year old liver transplant patient. In the hospital, he received 300 mg cyclosporin once a day as an iv infusion which resulted in a trough level of 175 ng/ml. After he is discharged, he will continue with oral cyclosporine treatment. Make a dose recommendation for DB.(10 points)

A. 150 mg every 12 hrs
B. 250 mg every 12 hrs
C. 500 mg every 12 hrs
D. 1000 mg every 12 hrs
E. 1500 mg every 12 hrs

If 300 mg cyclosporine provides correct plasma levels, dose simply needs to be converted to oral dose (F = 0.3)

\[ \text{New dose} = \frac{F_{\text{current}}}{F_{\text{NewFormulation}}} \times \text{Current dose} \]

\[ = \left( \frac{1}{0.3} \right) \times (300\, \text{mg}) = 1000\, \text{mg/day} \]

Give 500 mg every 12 hours.
6. Procainamide is metabolized to an active metabolite, ____________, and is formed by the process of _______________. (5 points)

A.) MEGX; alkylation
B.) MEGX; acetylation
C.) GX; acetylation
D.) NAPA; alkylation
E.) NAPA; acetylation
J.N. is a 72 year old, 58 kg male with cirrhosis of the liver. He is put on lidocaine therapy to treat his arrhythmia. Calculate a loading dose to achieve a concentration of 5 mg/L and a maintenance dose for a steady-state concentration of 2 mg/L. (10 points)

A.) Loading Dose = 200 mg; Maintenance Dose = 48 mg/hr
B.) Loading Dose = 766 mg; Maintenance Dose = 48 mg/hr
C.) Loading Dose = 167 mg; Maintenance Dose = 80 mg/hr
D.) Loading Dose = 167 mg; Maintenance Dose = 80 mg/hr
E.) Loading Dose = 200 mg; Maintenance Dose = 80 mg/hr

LD = (Vc *C)/S
Vc = 0.6*58 = 35 L

Loading Dose = (35 L*5 mg/L)/0.87 = 200 mg

Maint. Dose = (Cl *C)/S
Cl = 0.36*58 = 20.9 L/hr

MD = (20.9 L/hr *2 mg/L)/0.87 = 48 mg/hr
8. Which of the following changes goes along with a decreased clearance and no change in volume of distribution? (5 pts.)

A) shorter half-life, higher steady state concentration
B) longer time to steady state, shorter half-life
C) longer time to steady state, lower steady state concentration
D) increased initial concentration after an i.v. bolus, longer time to steady state
E) longer time to steady state, higher steady state concentration
9. Once daily aminoglycoside therapy rationale includes which of the following: (5 pts)

1. Treatment is more cost effective
2. Reduced toxicity due to lower peak concentrations
3. Reduction in post-antibiotic effect
4. Bacteria develop active resistance for 14-30 hours

A) 1, 2, 3, and 4
B) 1, 2 and 4
C) 1 and 4
D) 1, 3 and 4

a. 3 and 4
10. H.P., a 45-year-old, 70kg male, is to be started on Phenobarbital for his seizure disorder. Calculate the maintenance dose of sodium Phenobarbital that will produce a steady-state concentration of 30 mg/L. (5 points)

A. 201.6 mg/day sodium phenobarbital  
B. 448 mg/day sodium phenobarbital  
C. **224 mg/day sodium phenobarbital**  
D. 403.2 mg/day sodium phenobarbital  
E. 180 mg/day sodium phenobarbital

\[ MD = \frac{Cl \cdot Cpss \cdot \tau}{S \cdot F} \]

\[ = \frac{(4mL/kg/hr) \cdot 70kg \cdot (30mg/L) \cdot 24hr \cdot 1L}{0.9 \cdot 1 \cdot 1000ml \cdot 1day} \]

\[ = 224 \text{ mg/day} \]
11. Based on population average value, calculate a daily dose of phenytoin that will produce a steady-state phenytoin level of 15 mg/L in a 60 kg male. (5 points)

A. 305.1 mg/day phenytoin
B. **331.6 mg/day phenytoin**
C. 360.4 mg/day phenytoin
D. 378.3 mg/day phenytoin
E. 284.3 mg/day phenytoin

Population value:
Vmax = 7 mg/kg/day * 60 = 420 mg/day
Km = 4mg/L

\[ R_0 = \frac{V_m \cdot C}{(K_m + C)} = \frac{420 \cdot 15}{(4 + 15)} = 331.6 \text{mg/day phenytoin} \]
12. Your patient is admitted to the hospital after a major accident. He is 5’8” tall and at admission he weighed 70kg. His creatinine clearance is 120mL/min. The day following surgery he weighs 77kg and is suffering from an infection. At 8:00 am he is given a half an hour infusion of 350mg of gentamicin. What will his plasma concentration be at 2:30 pm? (10 pts)

- **a)** 2.3 μg/mL  
- **b)** 1.78 mg/L  
- **c)** 1.48 μg/mL  
- **d)** 2 μg/L  
- **e)** 1.54 mg/L

**Key:**

First calculate his ideal body weight.

\[ IBW = 50 + 2.3 \times 9 = 68.4 \text{ kg} \]

ESF = 77 – 70 = 7 L

\[ Vd = 0.25 (70) + 7 = 24.5 \text{ L} \]

For \( C_{\text{min}} \) at 2:30 pm you must first calculate \( C_{\text{max}} \). For this, you need the \( ke \). Since \( Cl=ClCr \), and you know 120mL/min=7.2 L/hr,

\[ ke = \frac{7.2}{24.5} = 0.29 \text{ hr}^{-1} \text{ or } ke = 0.00293(120) + 0.014 = 0.37 \]

\[ C_{\text{max}} = \frac{350}{7.2 \times 0.5} \times (1 - e^{-0.29 \times 0.5}) = 13.12 \text{ mg/L} \text{ or if } ke = 0.37 \ C_{\text{max}} = 16.4\text{mg/ml} \]

For \( C_{\text{min}} \),

\[ C_{\text{min}} = 13.12 e^{-0.29 \times 6} = 2.3 \text{ mg/L or if } ke = 0.37 \ C_{\text{min}} = 1.78 \text{ mg/L} \]
13. Mr. H.L. (65 years old, 72kg, SrCr = 1.5mg/L, CHF) was admitted to the hospital for digoxin toxicity. He had been taken 0.25 mg digoxin qd for 3 months. The digoxin plasma concentration was determined to be 5 μg/L. How many hours will it take for the concentration to fall back to 1.5μg/L? (5 points)

\[ \text{Cl}_{\text{cr}} = \frac{(140-65) \times 72}{72 \times 1.5} = 50 \text{mL/min} \]

\[ \text{Cl} = 0.33 \times 72 + 0.9 \times 50 = 68.76 \text{ mL/min} = 4.13 \text{ L/h} \]

\[ \text{Vd} = 3.8 \times 72 + 3.1 \times 50 = 428.6 \text{ L} \]

\[ \text{Ke} = \frac{\text{Cl}}{\text{Vd}} = 4.13/428.6 = 0.0096 \text{ h}^{-1} \]

\[ T = \frac{\ln(5/1.5)}{0.0096} = 125.4 \text{ h} = 125 \text{ h} \]

**a.125h**

b.147h
c.160h
d.96.8h
e.112h